

Application No. 10/530,794
Amendment Dated May 16, 2008
Reply to Office Action of February 20, 2008

The listing of claims will replace all prior versions and listings of claims in the application.

Listing of the Claims

Claim 1. (original) A combination, comprising an endothelin receptor antagonist, or a pharmaceutically acceptable salt thereof, and an EGFR TKI, or a pharmaceutically acceptable salt thereof.

Claim 2. (original) A combination according to claim 1 wherein the endothelin receptor antagonist is selected from A-127722, atrasentan (ABT-627), BQ-123, BQ-788, BMS 182874, feloprentan, BSF 420627, FR139317, IPI-950, L-749,329, L-754,142, LU 110896, LU 110897, PD 156707, PD 155080, Ro 46-2005, bosentan (Ro 47-0203), SB 217242, SB 209670, TAK-044, YM598, sitaxsentan (TBC11251), ambrisentan, tezosentan, darusentan, *N*-[[2'-[[(4,5-dimethyl-3-isoxazolyl)amino]sulphonyl]-4-(2-oxazolyl)[1,1'-biphenyl]-2-yl]methyl]-*N*,3,3-trimethylbutanamide, ZD1611 and *N*-(3-methoxy-5-methylpyrazin-2-yl)-2-(4-[1,3,4-oxadiazol-2-yl]phenyl)pyridine-3-sulphonamide (ZD4054), or a pharmaceutically acceptable salt thereof.

Claim 3. (previously amended) A combination according to claim 1 wherein the EGFR TKI is selected from:

N-(3-chloro-4-fluorophenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine (ZD1839); *N*-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine, or a pharmaceutically-acceptable salt thereof (linked to the code numbers CP 358774 and OSI-774 (the monomethanesulphonate salt));

6-acrylamido-*N*-(3-chloro-4-fluorophenyl)-7-(3-morpholinopropoxy)quinazolin-4-amine (linked to the code numbers PD 183805 and CI 1033);

4-[(1*R*)-1-phenylethylamino]-6-(4-hydroxyphenyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (linked to the code numbers PKI-166, CGP 75166 and CGP 59326);

N-[4-(3-bromoanilino)quinazolin-6-yl]but-2-ynamide (linked to the code numbers CL-387785 and EKB-785); and

4-(3-chloro-4-fluoroanilino)-3-cyano-6-(4-dimethylaminobut-2(*E*)-enamido)-7-ethoxyquinoline (EKB-569);

or a pharmaceutically acceptable salt thereof.

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Claim 4. (previously amended) A combination according to claim 1 wherein the endothelin receptor antagonist is selected from ZD4054, or a pharmaceutically acceptable salt thereof, and the EGFR TKI is selected from ZD1839, or a pharmaceutically acceptable salt thereof.

Claim 5. (cancelled)

Claim 6. (previously amended) A pharmaceutical composition comprising a combination according to claim 1, in association with a pharmaceutically acceptable diluent or carrier.

Claim 7. (previously amended) A method of treating cancer, in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a combination according to claim 1.

Claim 8. - 9. (cancelled)

Claim 10. (previously amended) The method according to claim 7 wherein the cancer is oesophageal cancer, myeloma, hepatocellular, pancreatic, cervical cancer, ewings tumour, neuroblastoma, kaposis sarcoma, ovarian cancer, breast cancer, colorectal cancer, prostate cancer, bladder cancer, melanoma, lung cancer - non small cell lung cancer (NSCLC), and small cell lung cancer (SCLC), gastric cancer, head and neck cancer, brain cancer, renal cancer, lymphoma and leukaemia.

Claim 11. (cancelled)

Claim 12. (withdrawn) The method according to claim 10 wherein the cancer is prostate cancer.

Claim 13. (previously amended) The method according to claim 10 wherein the cancer is NSCLC.

Claim 14. (previously amended) The method according to claim 10 wherein the cancer is in a metastatic state.

Claim 15. (previously amended) The method according to claim 10 wherein the cancer is in a non-metastatic state.

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Claim 16. (previously amended) The method according to claim 10 wherein the cancer is renal, thyroid, lung, breast or prostate cancer that is producing bone metastases.

Claim 17. (previously presented) A combination according to claim 2 wherein the EGFR TKI is selected from:

N-(3-chloro-4-fluorophenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine (ZD1839);

N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine, or a pharmaceutically-acceptable salt thereof (linked to the code numbers CP 358774 and OSI-774 (the monomethanesulphonate salt));

6-acrylamido-*N*-(3-chloro-4-fluorophenyl)-7-(3-morpholinopropoxy)quinazolin-4-amine (linked to the code numbers PD 183805 and CI 1033);

4-[(1*R*)-1-phenylethylamino]-6-(4-hydroxyphenyl)-7*H*-pyrrolo[2,3-*d*]pyrimidine (linked to the code numbers PKI-166, CGP 75166 and CGP 59326);

N-[4-(3-bromoanilino)quinazolin-6-yl]but-2-ynamide (linked to the code numbers CL-387785 and EKB-785); and

4-(3-chloro-4-fluoroanilino)-3-cyano-6-(4-dimethylaminobut-2(*E*)-enamido)-7-ethoxyquinoline (EKB-569);

or a pharmaceutically acceptable salt thereof.

Claim 18. (previously presented) A pharmaceutical composition comprising a combination according claim 17, in association with a pharmaceutically acceptable diluent or carrier.

Claim 19. (previously presented) A method of treating cancer, in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a combination according to claim 17.

Claim 20. (withdrawn) The method according to claim 19 wherein the cancer is prostate cancer.

Claim 21. (previously presented) The method according to claim 19 wherein the cancer is NSCLC.

Claim 22. (previously presented) The method according to claim 19 wherein the cancer is in a metastatic state.

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Claim 23. (previously presented) The method according to claim 19 wherein the cancer is in a non-metastatic state.

Claim 24. (previously presented) The method according to claim 19 wherein the cancer is renal, thyroid, lung, breast or prostate cancer that is producing bone metastases.